I. The Claimed Invention Is Sufficiently Enabled

A. Decreasing glucose/insulin levels

Claims 24-31 and 40-47 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to provide an enabling disclosure. Claims 25, 29, 41 and 45 have been canceled. Applicants traverse the rejections and request reconsideration of the same.

The Office Action asserts that although the claims drawn to decreasing blood glucose and or insulin levels in humans are allowable, undue experimentation is required to decrease blood glucose and or insulin levels in other animals. Although Applicants disagree, solely to advance prosecution of the present application, claims 24, 27, 28, 31, 40, 43, 44 and 47 have been amended to recite "human" instead of "animal". Accordingly, claims 24, 27, 28, 31, 40, 43, 44 and 47 are fully enabled. Furthermore, claims 26, 30, 42 and 46 depend from claims 24, 28, 40 and 44, respectively, and are also similarly enabled because these claims also recite "human".

The Examiner additionally rejected claims 40, 42-44, 46 and 47, which recite a method of "preventing or delaying" the onset of an increase in blood glucose or insulin, stating that the ability to decrease blood glucose levels or insulin levels in an organism comprising the administration of these antisense is not predictive of the ability to delay the onset or prevent increasing blood glucose or insulin level, and the "treatment effects demonstrated are not extrapolatable to prevention." (See pages 3 and 4 of the Office Action). Applicants respectfully disagree and assert that claims 40, 42-44, 46 and 47 are fully enabled by the specification.

The enablement requirement of §112 is satisfied so long as a disclosure contains sufficient information that persons of ordinary skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the following statement from *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971), is noteworthy:

> The only relevant concern of the Patent Office under these circumstances should be over the truth of any such assertion. The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the

> invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken as in compliance with the enabling requirements of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support. (emphasis added).

Throughout the specification, Applicants have clearly taught that an onset of an increase in glucose and or insulin levels may be prevented or delayed, and how such prevention or delay may be achieved. For example, Applicants have shown that the inhibition of nucleic acid molecules expressing PI3K p85 reduces glucose and insulin levels in vivo. (See Examples 21 and 22 of the specification). Since it has been shown that the decrease in expression of PI3K p85 correlates with the decrease in glucose and insulin levels, one of ordinary skill would expect that a increase in the level of expressed PI3K p85 would correlate with a increase in the level of glucose and insulin. Thus, a reasonable "extrapolation" can be made that if an antisense compound of claims 40, 42-44, 46 and 47 is administered to inhibit the expression of PI3K p85, the level of PI3K p85 would not be able to increase, and accordingly, an increase in the level of glucose and insulin would be **prevented** or **delayed**. Therefore, one of ordinary skill would understand that the present invention teaches that an onset of an increase in glucose and/or insulin may be prevented or delayed. Indeed, Applicants have shown that blood glucose and/or insulin levels can be decreased upon administration of a compound of the invention. Accordingly, there is no reason to believe that continued administration of the compounds would not prevent or delay an increase of blood glucose and/or insulin levels.

Throughout the specification, Applicants have also enabled one of ordinary skill to prevent or delay the increase in glucose and or insulin. For example, Applicants taught that the present invention provides for "methods of treating an animal, particularly a human, suspected of having or being prone to a disease or condition associated with expression of PI3K p85 by administering a therapeutically or **prophylactically** [i.e., preventing or delaying] effective amount of one or more of the antisense compounds...of the invention [i.e. the antisense compounds recited in claims 40, 42-44, 46 and 47]. (See page 5 of the specification). Moreover, Applicants taught that the claimed compounds may be administered in a number of ways, e.g., topical, inhalation, intratracheal, intranasal, epidermal, etc. (see page 23 of the specification); and

the dosage can be determined by one of ordinary skill in the art, e.g., 0.01 ug to 100 g per kg of body weight (see page 47 of the specification).

Additionally, the Applicants even clearly provided examples of how to practice the claimed methods of preventing an onset of an increase of glucose and or insulin. For example, on page 47 of the specification, Applicants taught that:

> "Following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the disease state, wherein the oligonucleotide is administered in maintenance doses, ranging from 0.01 ug to 100 g per kg of body weight, once or more daily..."

Applicants submit that there is no reason to doubt the objective truth of the statements contained in the application. Therefore, the Examiner **must** take Applicants' teaching of methods of preventing or delaying the onset of increase in glucose and/or insulin level as being in compliance with the enabling requirements of the first paragraph of §112. *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971).

Thus, claims 40, 42-44, 46 and 47 are fully enabled. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

II. Conclusion

Pending claims 24, 26-28, 30, 31, 40, 42-44, 46 and 47 are in condition for allowance and an early notice of the same is earnestly solicited. If, for any reason, the present application fails to proceed to allowance, the Examiner is encouraged to contact Applicants' undersigned representative at (215) 665-2158.

Respectfully submitted,

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